

REPRODUCTION SYSTEM MODULE

SESSION :2, LECTURE: 1

DURATION: 1hr

THE HYPOTHALAMUS-PITUITARY- GONAD AXIS

Module staff:

Dr Hadeel S. Al Ali

Dr Raya Muslim Alhassan (module leader)

Dr Nada Hashim Aljassim

Dr Nawal Mustafa Abdulah

Dr Nehaya Mnahi Al-Aubody

Dr Nesreen Muhsin Jar alla



Guyton, A.C., Human Physiology and Mechanisms of Disease, 13th Edition,
W.B. Saunders, 2016, ISBN: 978-1-4557-7005-2.



For more discussion, questions or cases need help please post to the session group





Learning Objectives (LO)

(LO1)

- List the hormones involved in reproduction produced by the hypothalamus the anterior and posterior pituitary glands and the gonads.

(LO2)

- List which cell types in the anterior pituitary gland produce which hormones.

(LO3)

- Describe the control of gonadotrophin secretion by the hypothalamus.





Learning Objectives (LO)

(LO4)

- Describe the action of gonadotrophins on the testes and ovaries.

(LO5)

- List the action of the gonadal steroids in the female and male.

(LO6)

- Describe the changes occurring in the ovary during the ovarian cycle and describe the changes in the endometrium.



Learning Objectives (LO)

(LO7)

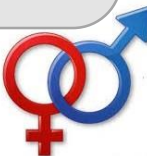
- List the phases of the menstrual cycle.

(LO8)

- Describe the pattern of secretion of gonadotrophins and gonadal steroids over the normal menstrual cycle.

(LO9)

- Describe the hypothalamic and pituitary mechanisms underlying cyclical gonadotrophin secretion and the interactions between the ovaries and hypothalamus/pituitary.





Learning Objectives (LO)

(LO10)

- List the actions of oestrogen and progesterone in the non-pregnant woman.

(LO11)

- Describe the effects of testosterone in the male.

(LO12)

- Explain how testosterone release is regulated by feedback control.





Learning Objectives (LO)

(LO13)

- Synthetic pathway of the gonadal steroids.



Hypothalamus-pituitary-gonadal axis

The major
controlling
structures
(♂ & ♀)

Brain (the
hypothalamus)

The pituitary
gland

The gonads
(testes or ovaries)

- ❖ In the pregnant female, important control is also exerted by the placenta.



What are the hormones involved in (LO1) reproduction?

1- Hypothalamus

1. Gonadotrophin-releasing Hormone (GnRH).

2. Thyrotropin-releasing hormone (TRH).

3. Prolactin-inhibiting hormone (PIH).



2- Pituitary gland

(LO1)

A- Anterior pituitary lobe

1. Luteinizing hormone (LH).

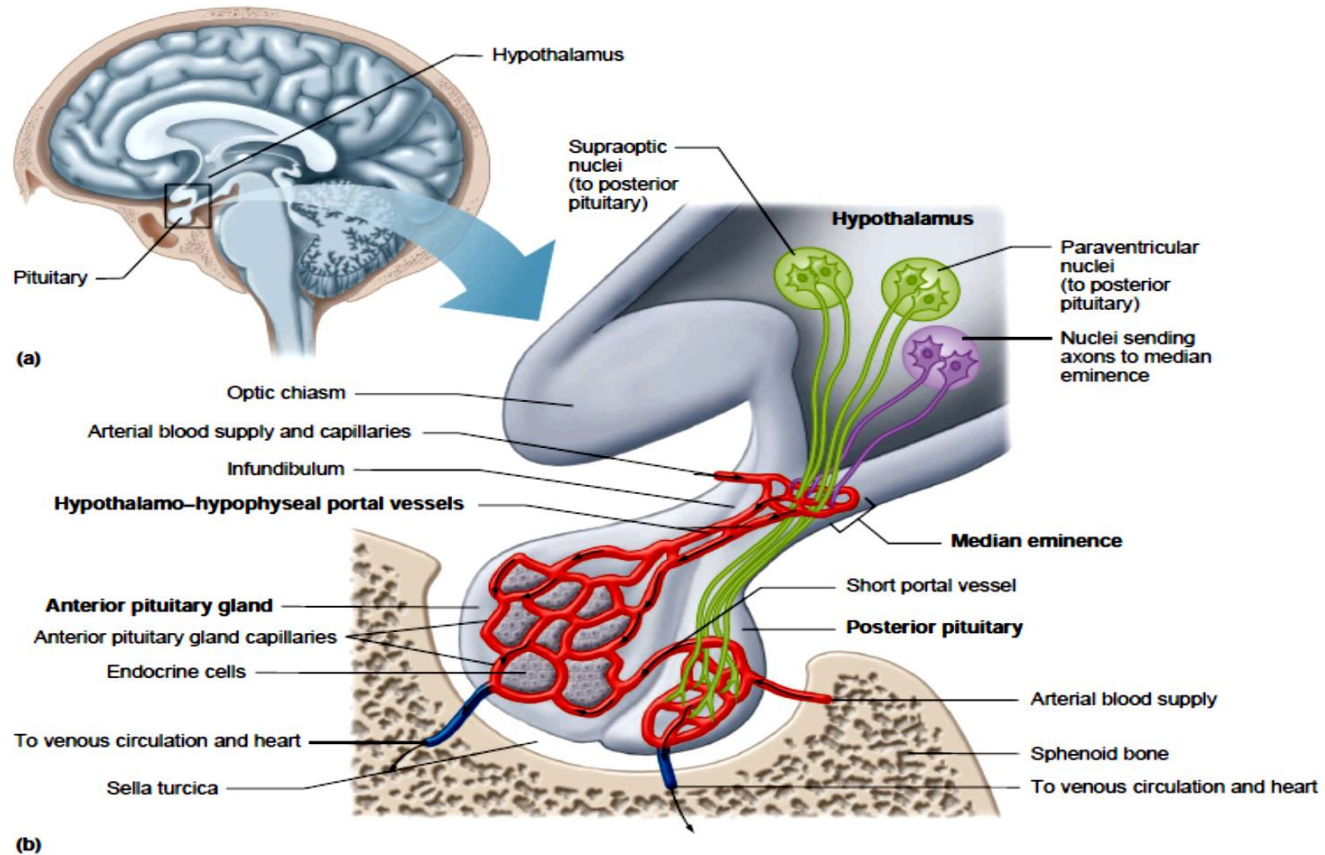
2. Follicle-stimulating hormone (FSH).

3. Prolactin.



B- Posterior pituitary lobe

- **Oxytocin.**



3. Gonads

(LO1)

A- Testes

1. Testosterone.

2. Inhibin.

**3. Mullerian inhibiting hormone
(MIH).**



B- Ovaries

1. Oestrogen.

2. Progesterone.

3. Inhibin.



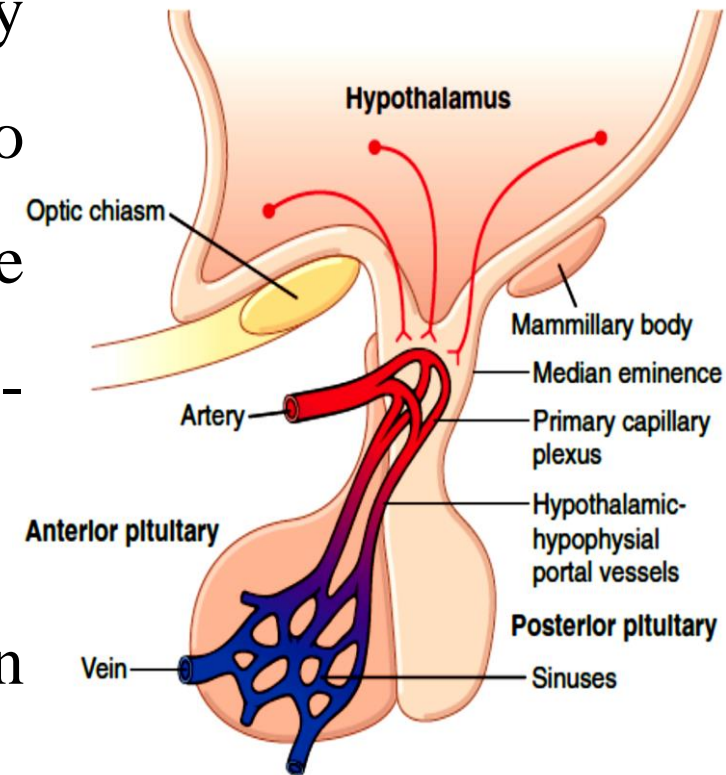
Cell types in the anterior pituitary gland

Hormone	Secreted by Cell Type	Chemical Structure	Main Target Tissue	Principle Actions
Follicle Stimulating Hormone (FSH)	Gonadotrophs	Peptide	Gonads	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis
Luteinising Hormone (LH)	Gonadotrophs	Peptide	Gonads	Causes ovulation and formation of the corpus luteum in the ovary; stimulates production of oestrogen and progesterone, stimulates testosterone
Thyroid Stimulating Hormone (TSH)	Thyrotropes	Peptide	Thyroid Gland	Secretion of thyroid hormones
Adrenocorticotrophic hormone (ACTH)	Corticotropes	Peptide	Adrenal Gland	Secretion of glucocorticoid, mineralocorticoid and androgens
Melanocyte Stimulating Hormone (MSH)	Corticotropes	Peptide	Melanocytes in Skin and Hair	Production and release of melanin
Growth Hormone	Somatotropes	Peptide	Liver, adipose tissue	Stimulates (body growth, secretion of insulin-like growth factor-1; lipolysis), inhibits actions of insulin on carbohydrate and lipid metabolism
Prolactin	Lactotropes	Peptide	Ovaries, mammary glands	Stimulates milk secretion and production



Control of gonadotrophin secretion

- Secretion of gonadotrophin hormones (LH and FSH) by the anterior pituitary is controlled by GnRH → conducted to the anterior pituitary through minute blood vessels called hypothalamic-hypophysial portal vessels.
- In the anterior pituitary, GnRH act on the glandular cells to control its secretion.

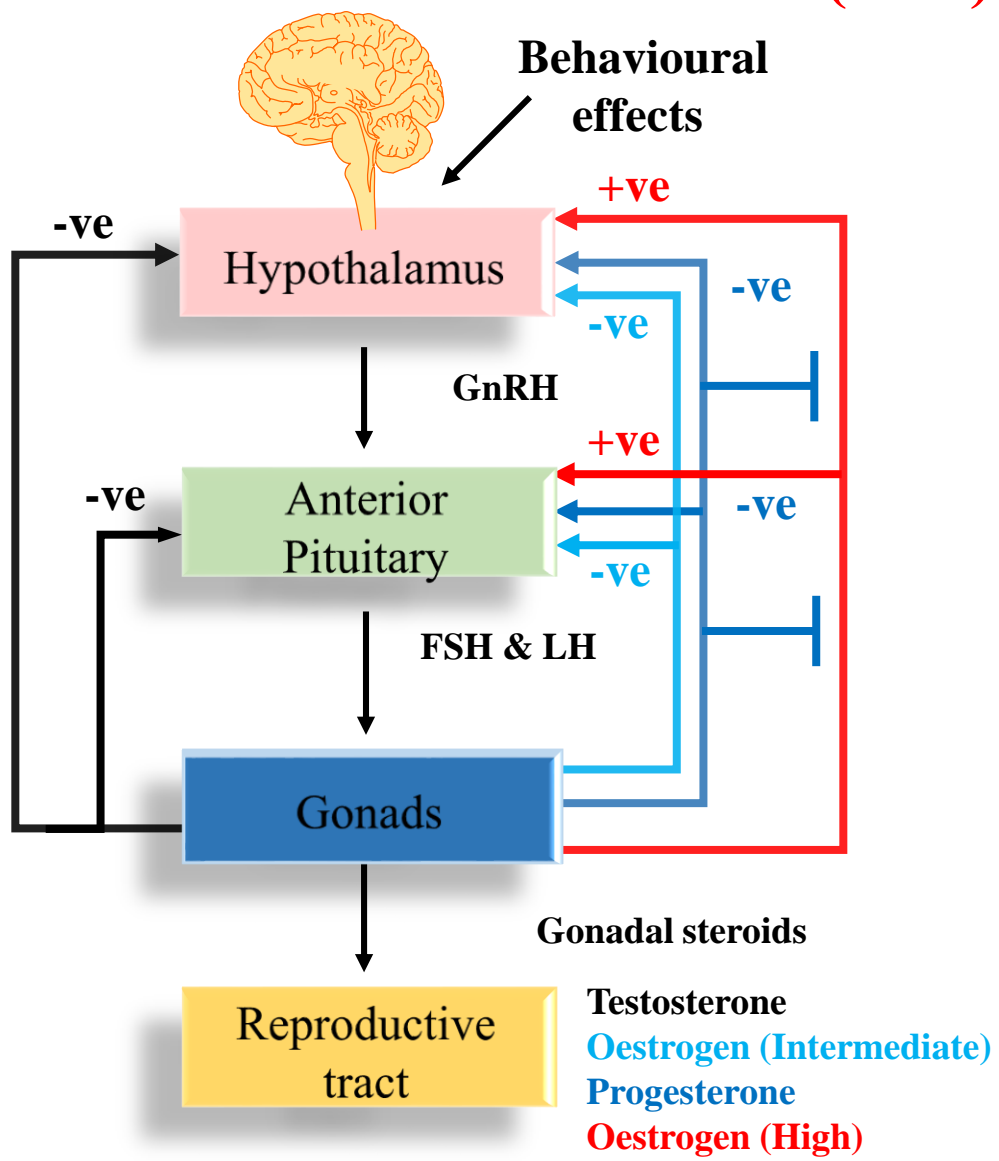


- Several groups of hypothalamic neurones secrete GnRH in a pulsatile manner (once an hour). Secretion of GnRH is under the influence both of other structures in the brain (environment via sensory input), body weight and circulating hormones.



Gonadal steroid hormones

- ❑ **Testosterone:**
reduces GnRH secretion
- ❑ **Oestrogen (intermediate conc.):**
reduces secretion
lowers amount secreted per pulse
- ❑ **Progesterone:**
increases the inhibitory effect of oestrogen
lowers the frequency of the pulses
- ❑ **Oestrogen alone (at high conc.):**
promotes the release of GnRH, producing a “surge”
- ❑ **Progesterone:**
prevents high levels of oestrogen producing a GnRH surge



- Gonadotrophs in the anterior pituitary secrete gonadotrophins LH & FSH in response to GnRH pulses.
- Absence of GnRH → no FSH or LH is secreted.
- The amount of FSH secreted in response to GnRH is reduced by **inhibin** (negative feedback inhibitor of FSH secretion), a glycoprotein hormone released by:
 - Granulosa cells of the ovary (follicle development), inhibits secretion of FSH.
 - Sertoli cells of the testis (seminiferous tubules), inhibits FSH secretion when rate of sperm production is sufficient.



Action of gonadotrophins on the testes and ovaries

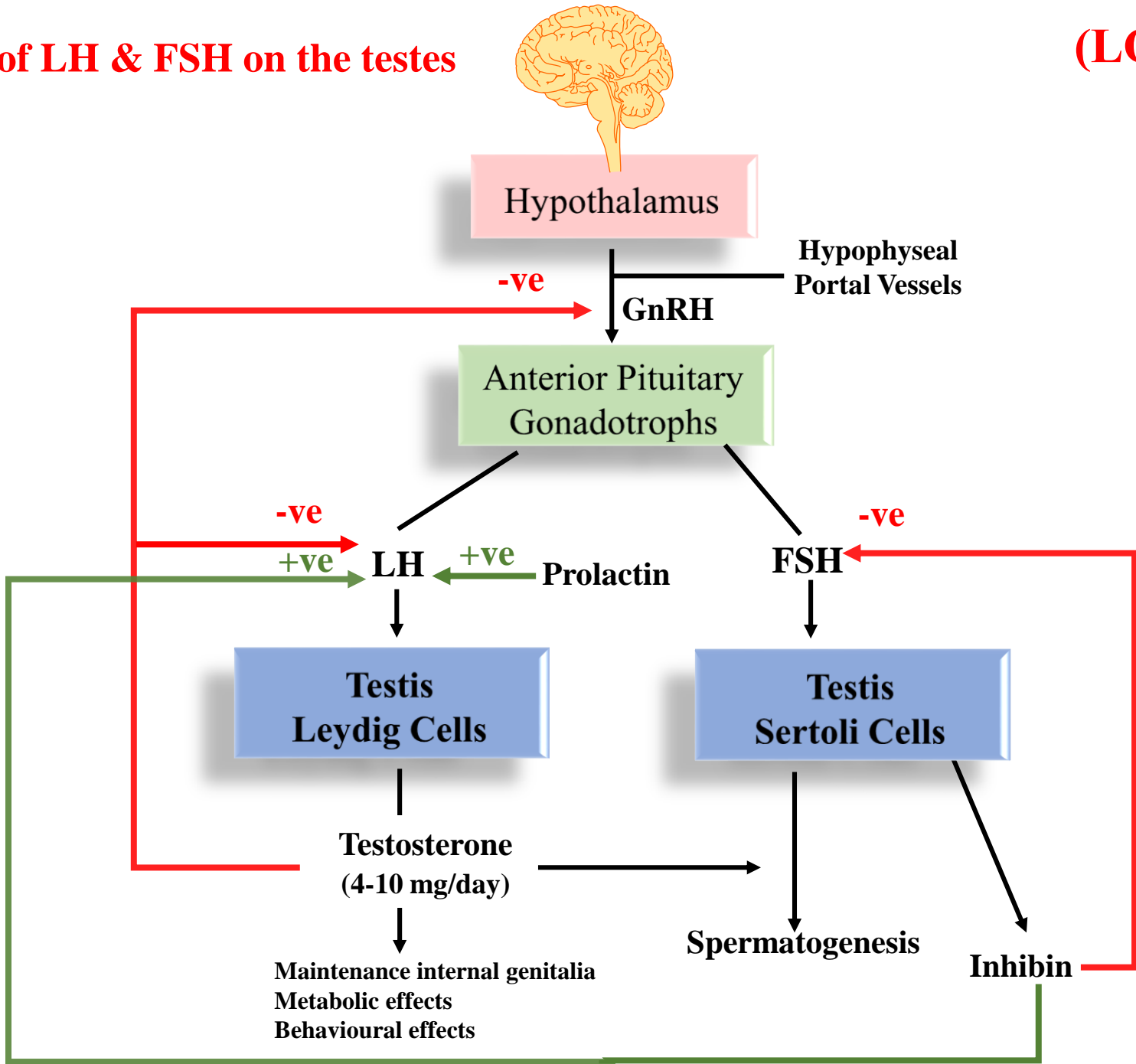
Testes

- **LH** stimulates Leydig cells (interstitial cells) of the testes to secrete androgens (sex steroid hormones) mainly testosterone (4-10mg/day). The effects of LH are enhanced by prolactin and inhibin.
 - **Testosterone** in turn acts on Sertoli cells to promote spermatogenesis and it also acts on other parts of the body to maintain the reproductive system.
- **FSH** causes sperm maturation in Sertoli cells of testes.



Action of LH & FSH on the testes

(LO4&12)



How testosterone release is regulated by feedback control?

(LO12)

- If testosterone levels rise:
 - GnRH secretion is inhibited (reduced LH and FSH)
 - LH and FSH are reduced further by testosterone (reducing sensitivity of gonadotrophs to GnRH)
→ so testosterone levels fall back
- If spermatogenesis proceeds too rapidly, inhibin levels rise
 - Inhibin reduces secretion of FSH by acting on the gonadotrophs



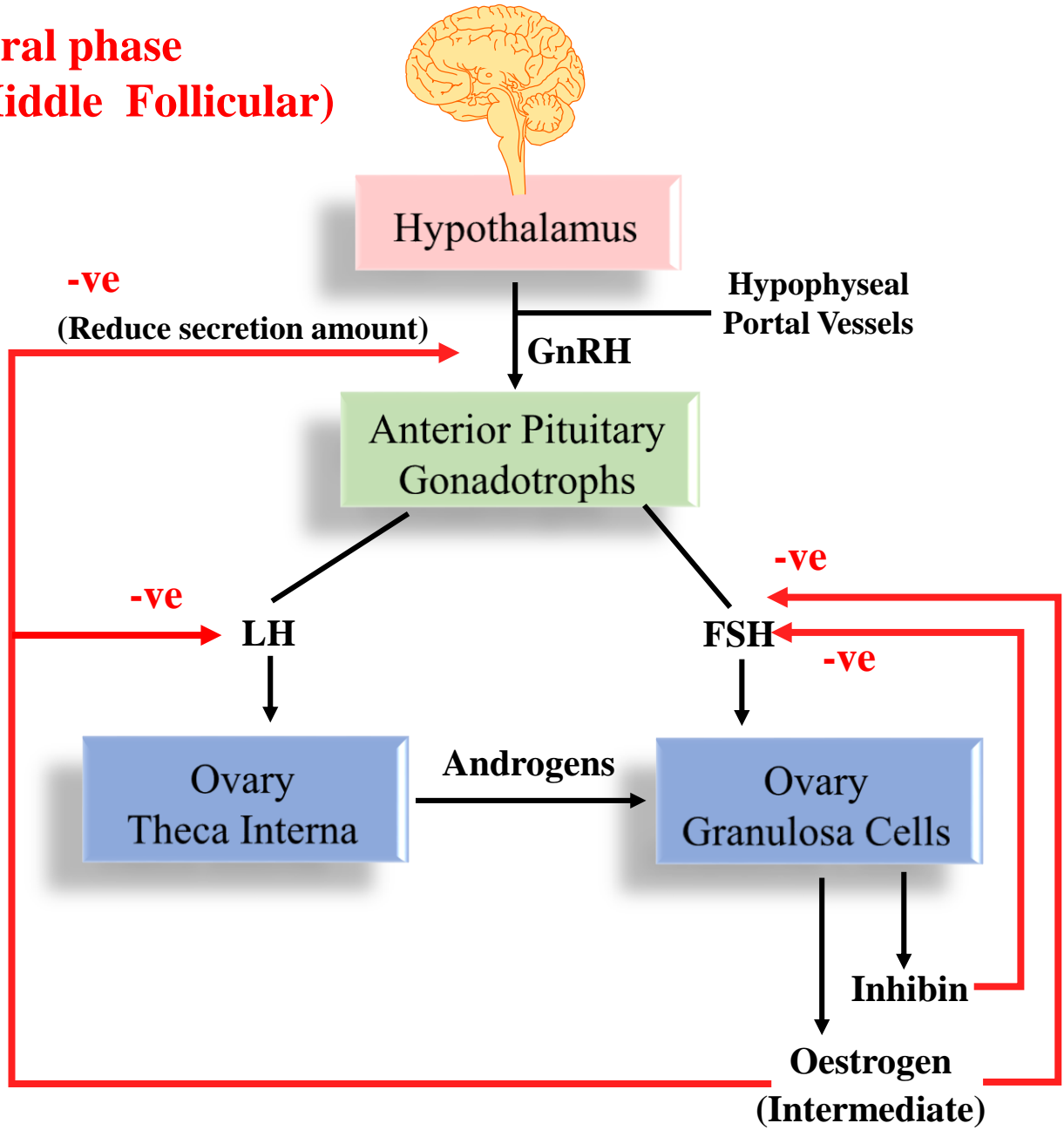
1- Antral Phase

- LH binds to theca interna cells and stimulates them to produce hormones, androgens (principally androstenedione).
- FSH binds to granulosa cells, FSH causes the biochemical change in the androgens via the thecal cells, to convert the androgens into oestrogens.

As the follicle grows more oestrogens are produced for a given gonadotrophic stimulation.



Antral phase (Early & Middle Follicular)

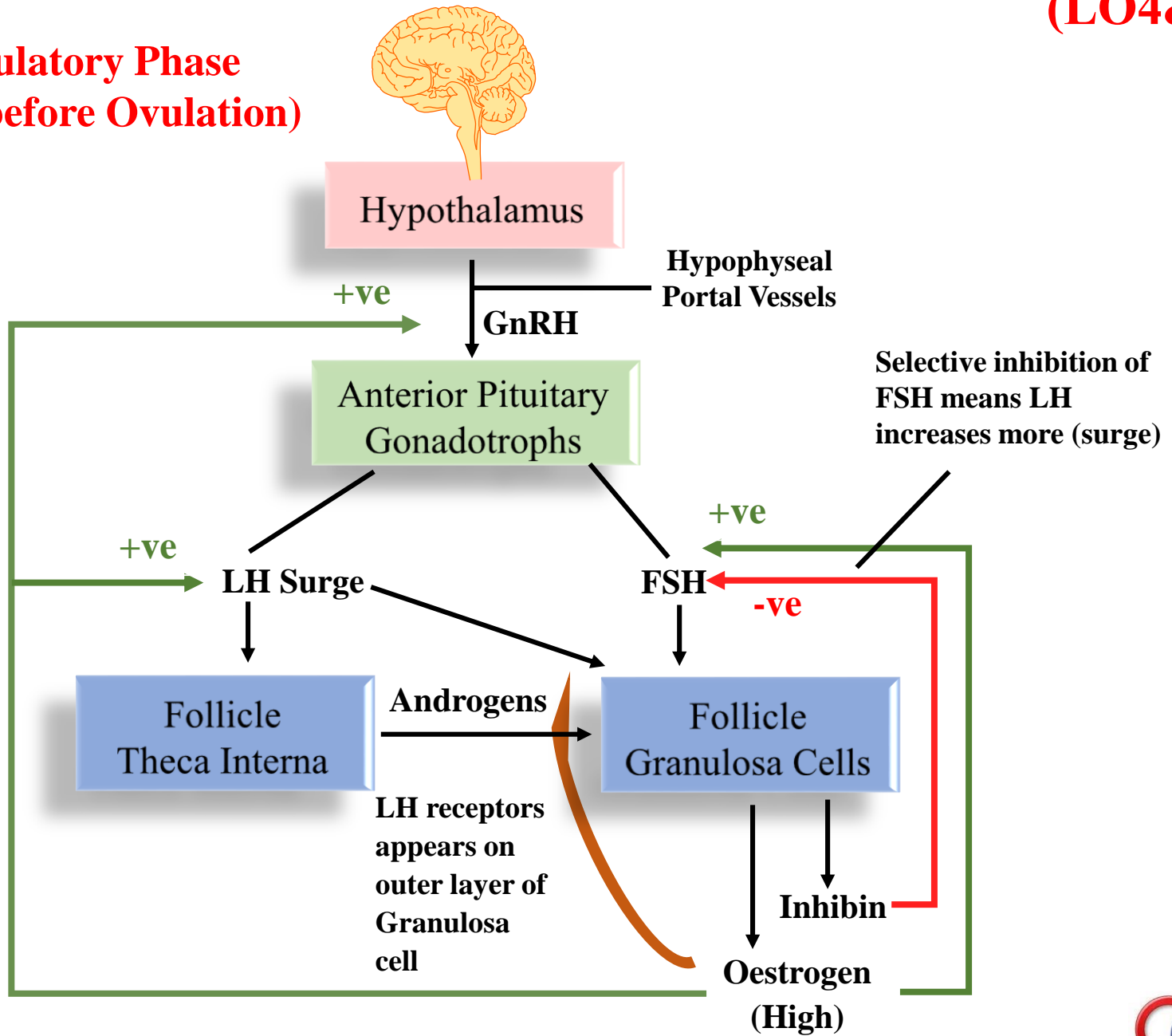


2- Pre-Ovulatory Phase

- Granulosa cells begin to express LH receptors.
- The rate of secretion of LH increases markedly (6-10) folds, FSH also increases about (2-3) fold at the same time.
- LH surge stimulates these receptors causing rapid changes in the follicle (will stimulate ovulation).
- The FSH and LH act synergistically to cause rapid swelling of the follicle.
- LH stimulates collagenase activity leading to rupture of follicle.
- High levels of oestrogen have a positive feedback effect on the secretion of FSH.
- FSH still being inhibited by inhibin.



Pre-Ovulatory Phase (37 hours before Ovulation)



(Follicle has grown, producing more)

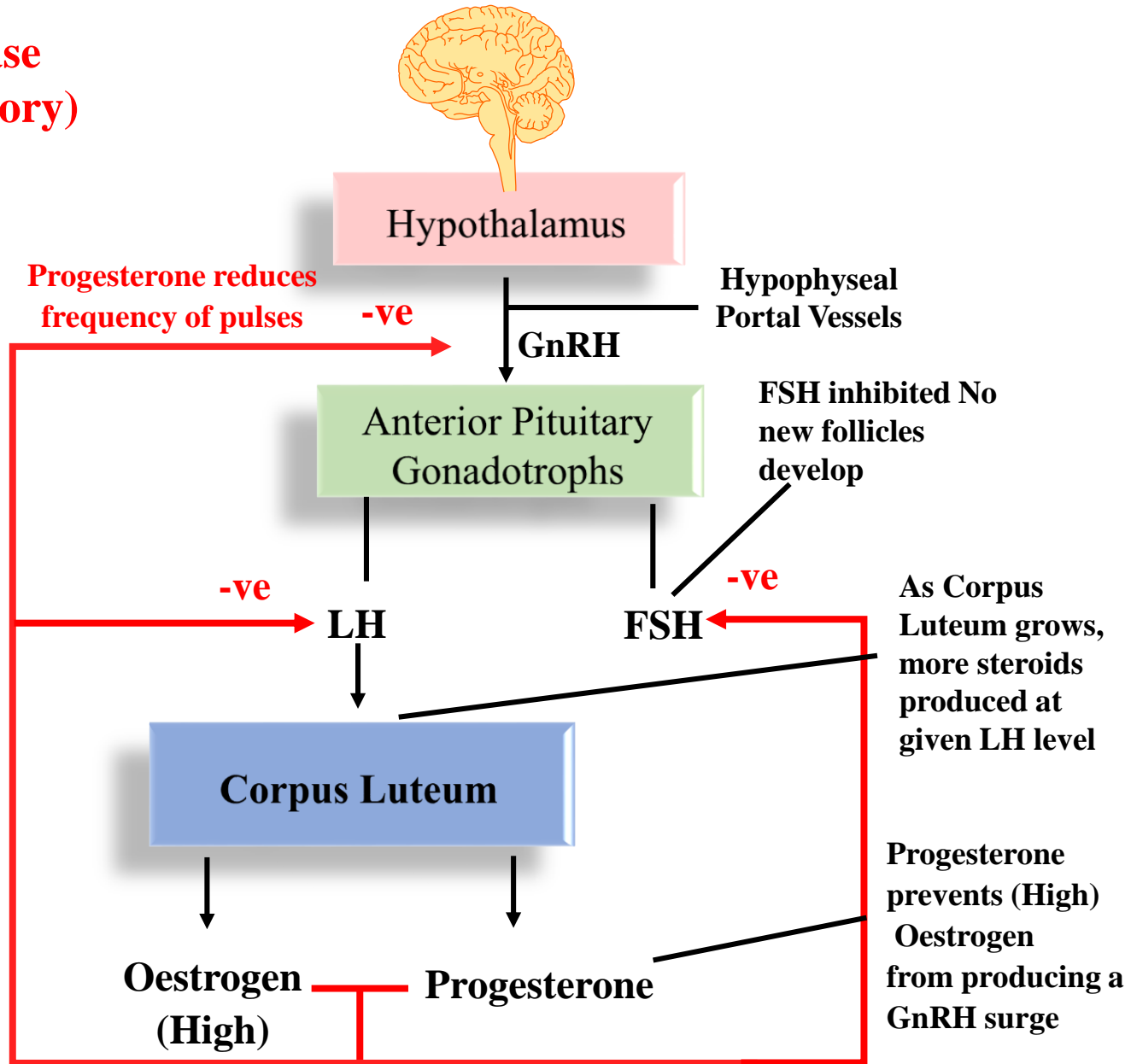


3- Luteal Phase

- The remaining granulosa and theca interna cells change (is dependent mainly on LH) rapidly into lutein cells (after expulsion of the ovum) → corpus luteum (luteinization).
- The corpus luteum secretes large amounts of both progesterone and oestrogen.
- These hormones have strong feedback effects on the anterior pituitary gland to maintain low secretory rates of both FSH and LH.
- The lutein cells secrete inhibin, this hormone inhibits FSH secretion.
- Low blood conc. of both FSH and LH result, and loss of these hormones causes the corpus luteum to degenerate completely.



Luteal phase (Post Ovulatory)

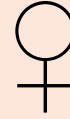


Action of the gonadal steroids in the female & male

Determinative effects are qualitative and only partly reversible if it all, these are mostly secondary sexual characteristics such as deepening of the voice.

Regulatory Effects are highly reversible, and rely on continuous hormonal stimulation for their maintenance.





Synergistic effect

Antagonistic effect

Intermediate conc.

Oestrogen reduces secretion of GnRH

Progesterone ↑ the inhibitory effect of oestrogen

Moderate

Oestrogen reduces the amount of GnRH secreted/pulse

Progesterone ↓ the frequency of pulses

High conc.

Oestrogen alone promotes release of GnRH “surge”

Progesterone prevents oestrogen producing surge



Actions of Testosterone

(LO5&11)

A- Determinative

↑ muscular growth, vocal cords, bones

↑ growth of body hair

Deepening of the voice

↑ Stature

Growth of the penis

B- Regulatory

Maintenance of the internal genitalia

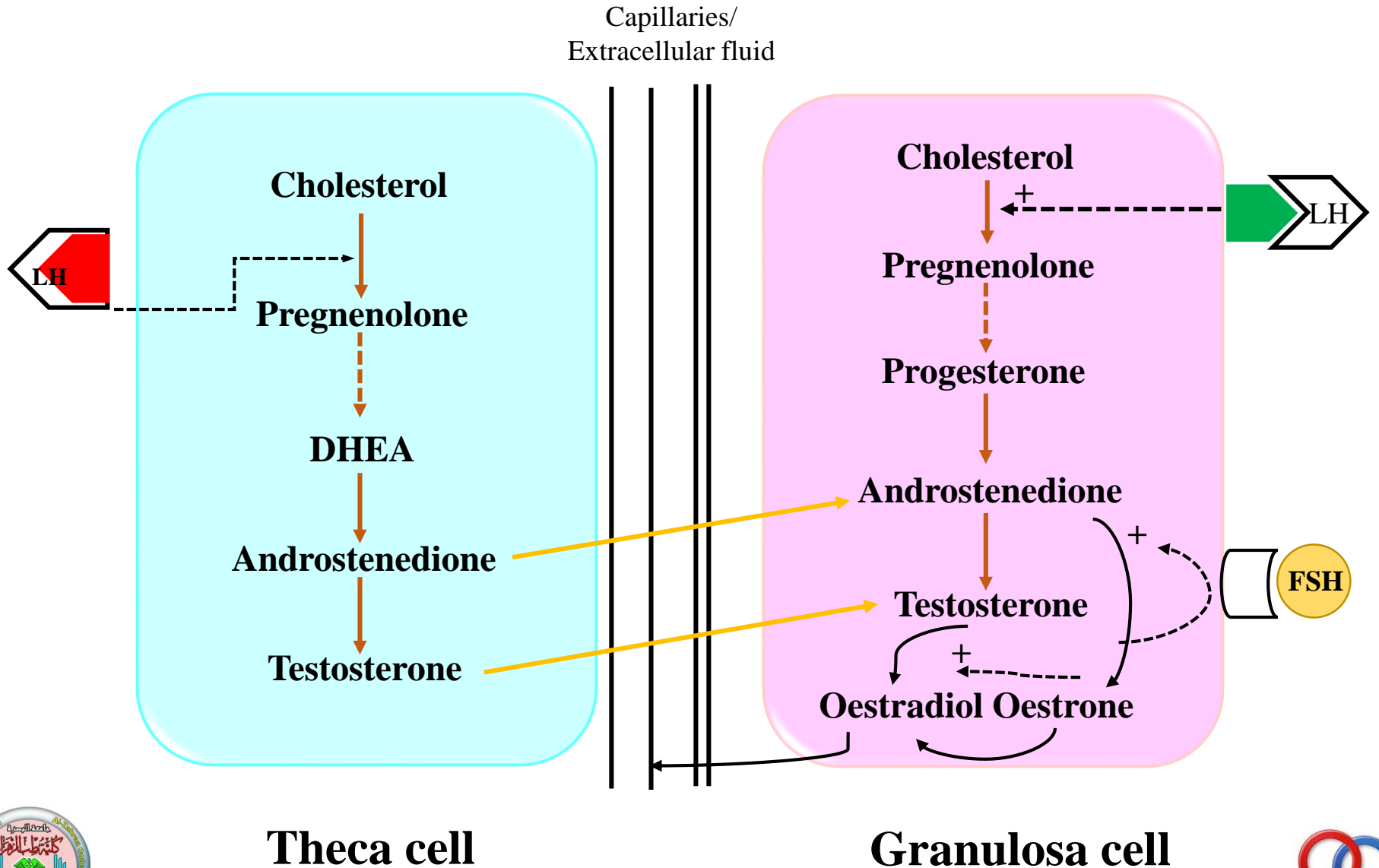
↑ the rate of cellular metabolism

Stimulates sexual activity



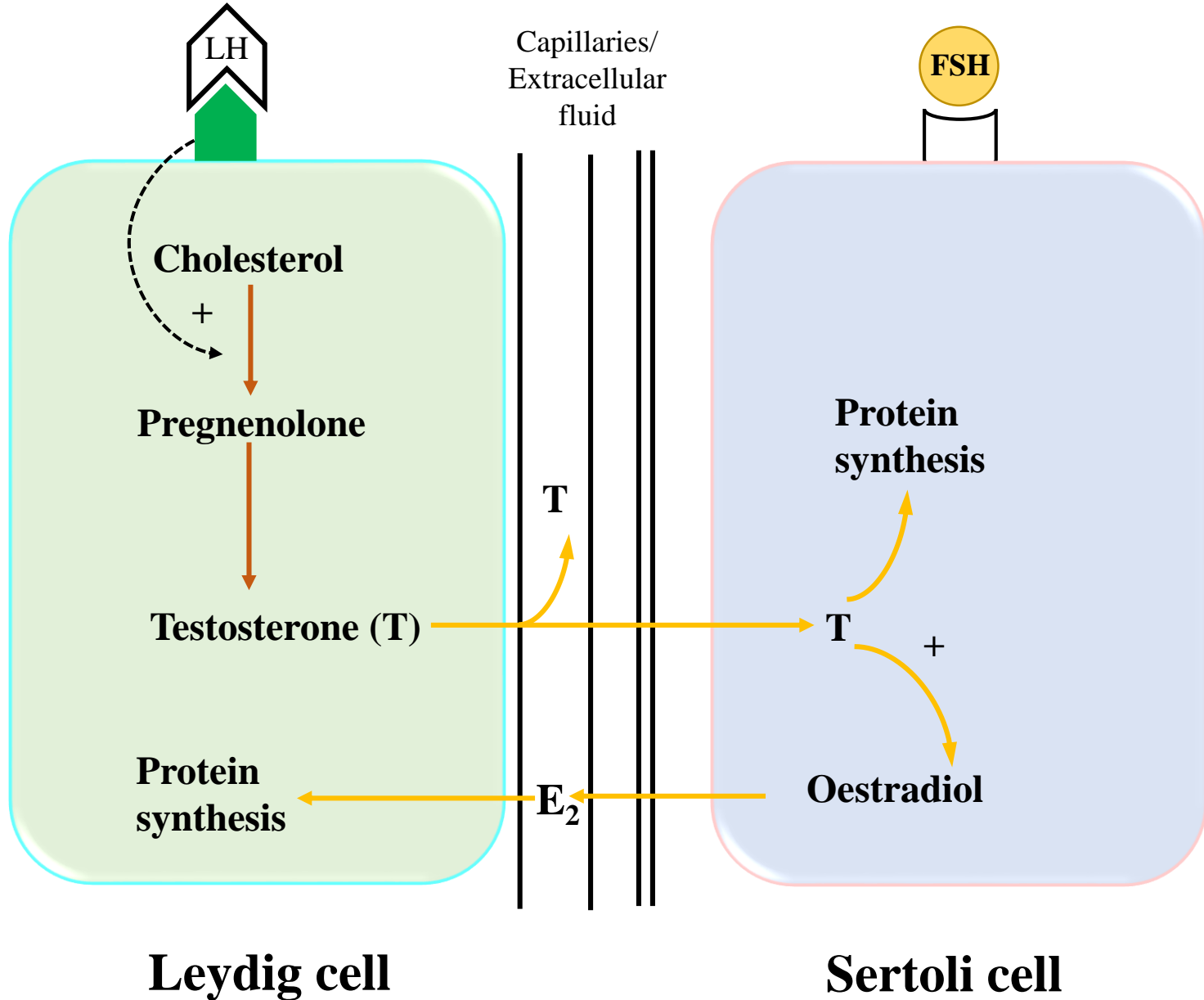
Oestrogen and progesterone synthesis

(LO13)



Testosterone synthesis

(LO13)



Thank you

